

**FIG. 1**

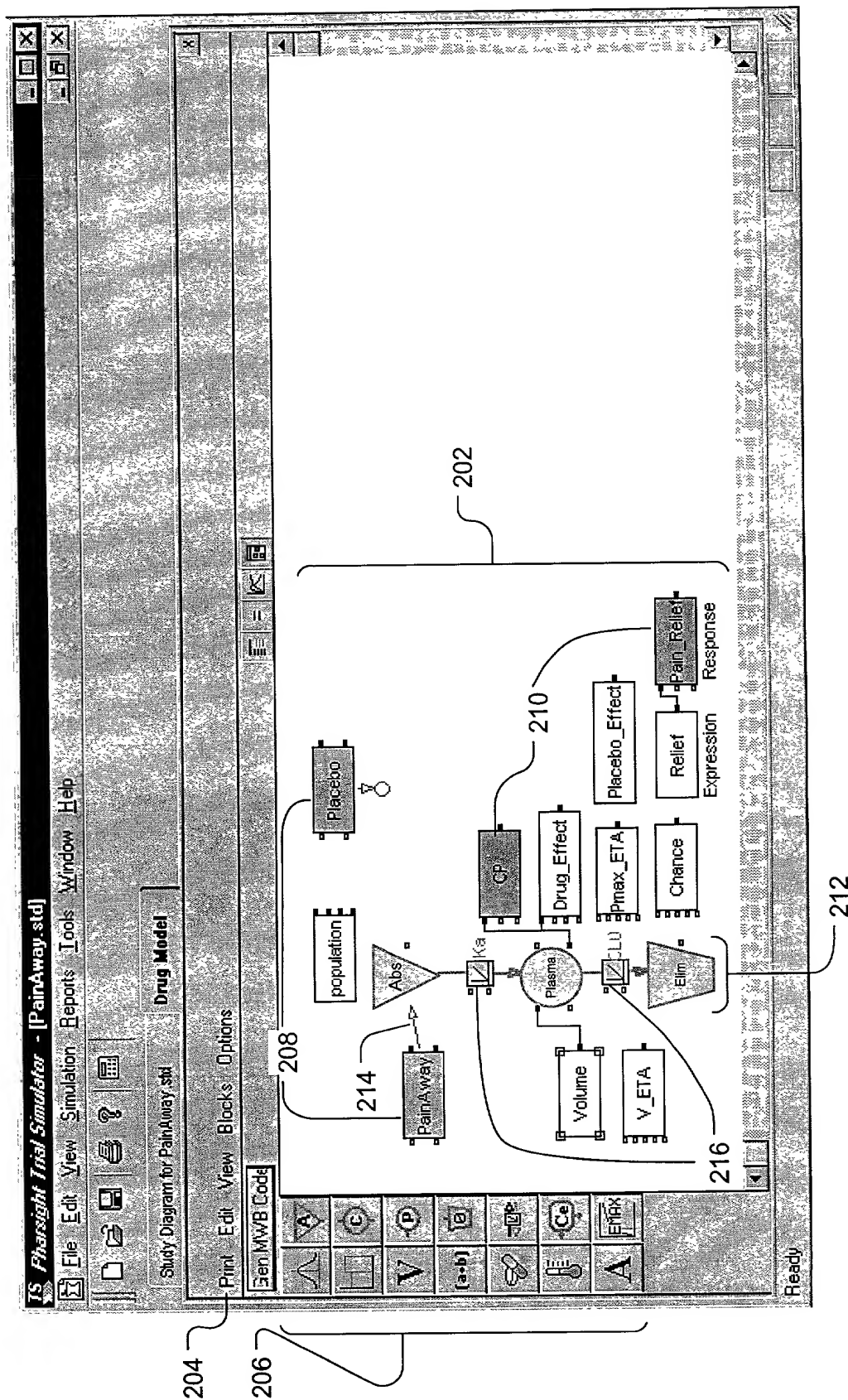


FIG. 2A

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**Block Properties**

Population: population

Covariates Distributions Continuous

Put covariates into joint distributions by clicking to include/exclude:

	BodyWeight	Gender	Age	creatinineClearance
Distribution: BodyWeight	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Distribution: Gender	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Distribution: Age	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Distribution: CreatinineClearance	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Comment:

260

**Block Properties**

Population: population

Covariates Distributions Continuous

Put covariates into joint distributions by clicking to include/exclude:

	BodyWeight	Gender	Age	creatinineClearance
Distribution: BodyWeight X Age	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Distribution: Gender	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Distribution: CreatinineClearance	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Comment:

☐ Show block type?

**FIG. 2B**

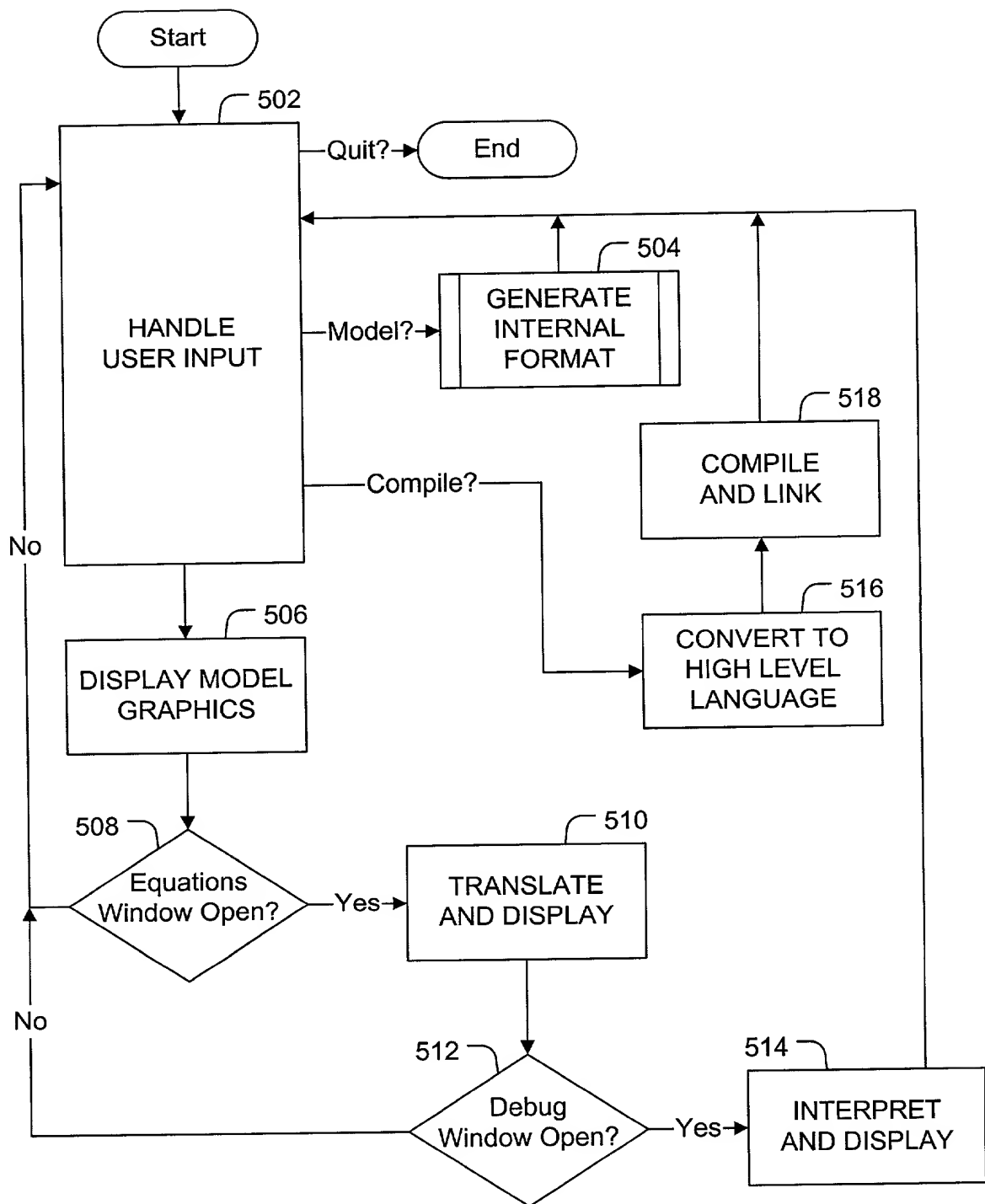


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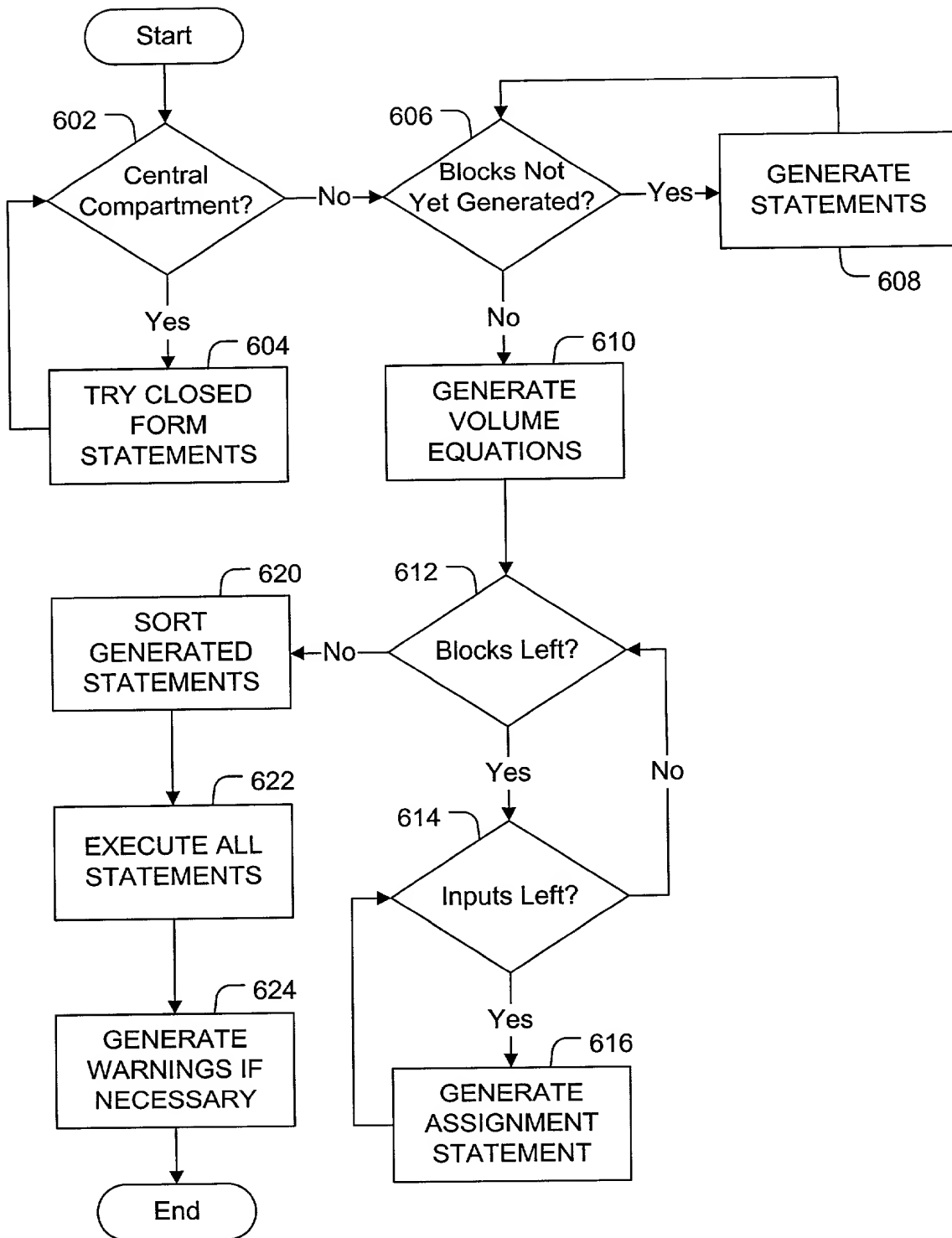
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Const	a numeric constant
NamedConst	a numeric constant having a name, such as Male or Female
StrConst	a string constant such as 'this is a string'
Unit	a basic unit such as L(liters) or d(days)
GetPort	a reference to the value of a variable
Trinop	trinary operator, such as the conditional operator
Binop	binary operator, such as +, -, *, /, comparison, etc.
Unop	unary operator, such as unary minus, and logical .not.
TimesUnit	multiplication by a unit phrase
UnitBinop	binary unit operator, such as *, /
UnitPhrase	encapsulates a unit phrase
DelayFunc	the delay function. It's output equals its input delayed by an offset.
TableFunc	the tabular function.
Funcall	calls one of a set of built-in functions, such as sqrt, exp, ln, etc.
SetPort	stores a value into a variable
SetDerv	sets the derivative (rate of change) of a variable
DEvent	represents the action to be performed when an event fires.
CDistr	represents a univariate continuous distribution.
DDistr	represents a univariate categorical distribution.
DLogit	represents a categorical distribution determined by an input value, some offset values, and a link function.
Choose	represents block equivalent of the trinary conditional expression.
Subrcall	represents a call to an external user-written subroutine.
NewStmtSequence	represents a sequence of statements
StmtIfThenElse	represents an if-then-else statement
InitCF	initializes a closed form machine by setting its initial parameters.
Add1stOrdCF	modifies a closed form machine by convolving its parameters with a first order delay.
Add1stOrdInputCF	modifies a closed form machine by convolving its parameters with a first order delay.
CloneCF	copies one closed form machine into another.
GetValCF	reads the value of a closed form machine
AddDoseCF	adds a bolus dose to a closed form machine
AddRateCF	adds to the infusion rate in a closed form machine
IfLevel	a special if statement used to guard statements, causing them to only be executed at the proper distribution level, such as continuous, event, periodic, etc.
SetDiscrete	used to set a group of categorical variables that are jointly distributed.
DSwitch	used to choose among a set of continuous values on the basis of a set of discrete values.
MCorDistr	represents a multivariate continuous distribution with correlation matrix
MVarDistr	represents a multivariate continuous distribution with variance-covariance matrix.
MVarImport	represents a set of variables that are being imported.

**FIG. 4**



**FIG. 5**



**FIG. 6**

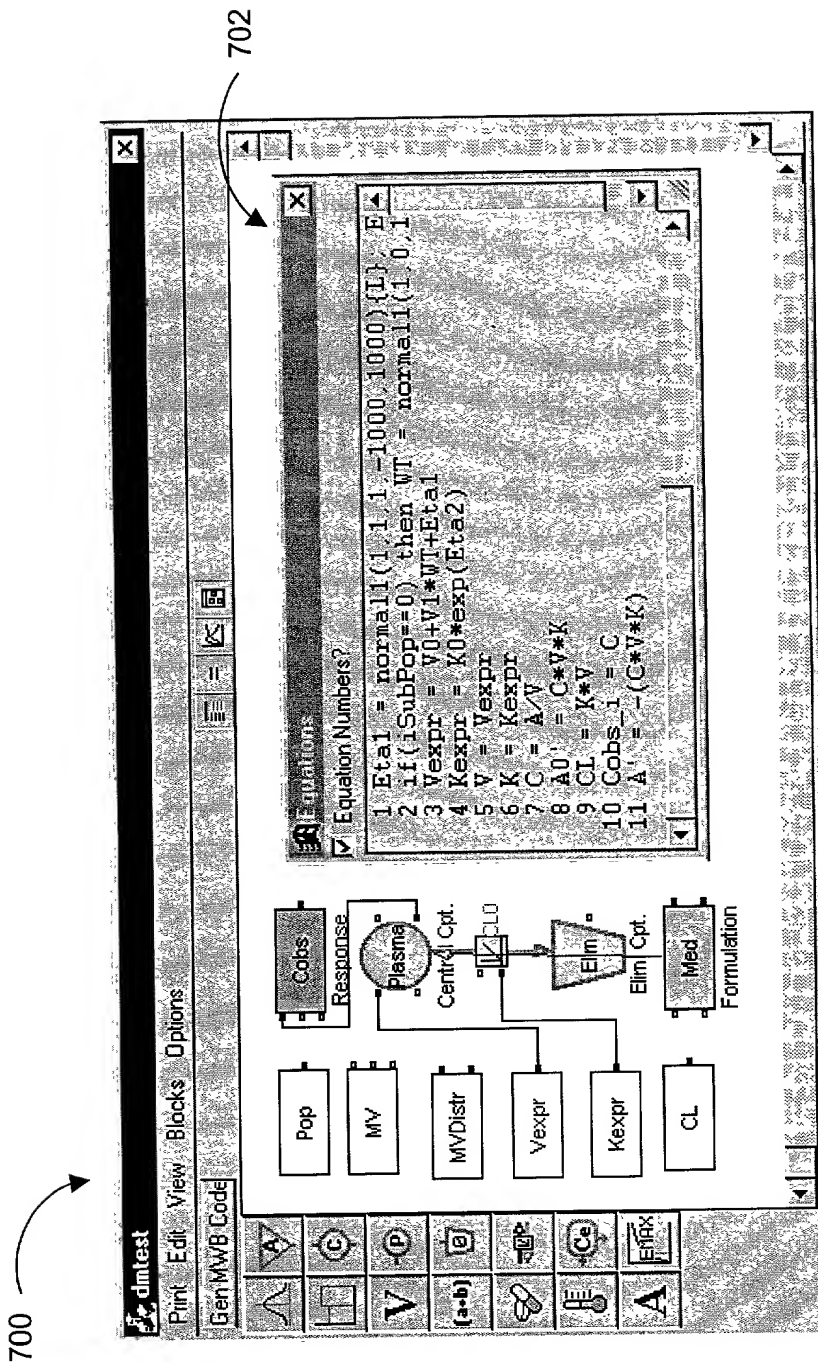


FIG. 7A



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1 if (iSubPop=0) then switch(SetDiscretel(ddistr(2, 0.51, 0.49), Gender, 2), BodyWeight = no;
2 A = -(A*Ka)
3 Temp_00 = normal(1, V_ETA_mean, V_ETA_sd, V_ETA_lo, V_ETA_hi)
4 V_ETA = V_ETA_mult*Temp_00
5 Volume = BodyWeight*1(L/kg)
6 Temp_01 = normal(1, Pmax_ETA_mean, Pmax_ETA_sd, Pmax_ETA_lo, Pmax_ETA_hi)
7 Pmax_ETA = Pmax_ETA_mult*Temp_01
8 Placebo_Effect = 0.3
9 Temp_02 = uniform(1, Chance_lo, Chance_hi)
10 Chance = Chance_mult*Temp_02
11 Relief = 1
12 V = Volume
13 Pain_Relief_1 = Relief
14 C = A1/V
15 A0 = C*Cl
16 CP_1 = C
17 Drug_Effect_C = C
18 A1 = A*Ka-C*Cl
19 Drug_Effect = Drug_Effect_Emax*Drug_Effect_C**Drug_Effect_Hi1/(Drug_Effect_EC50**Drug_Ef

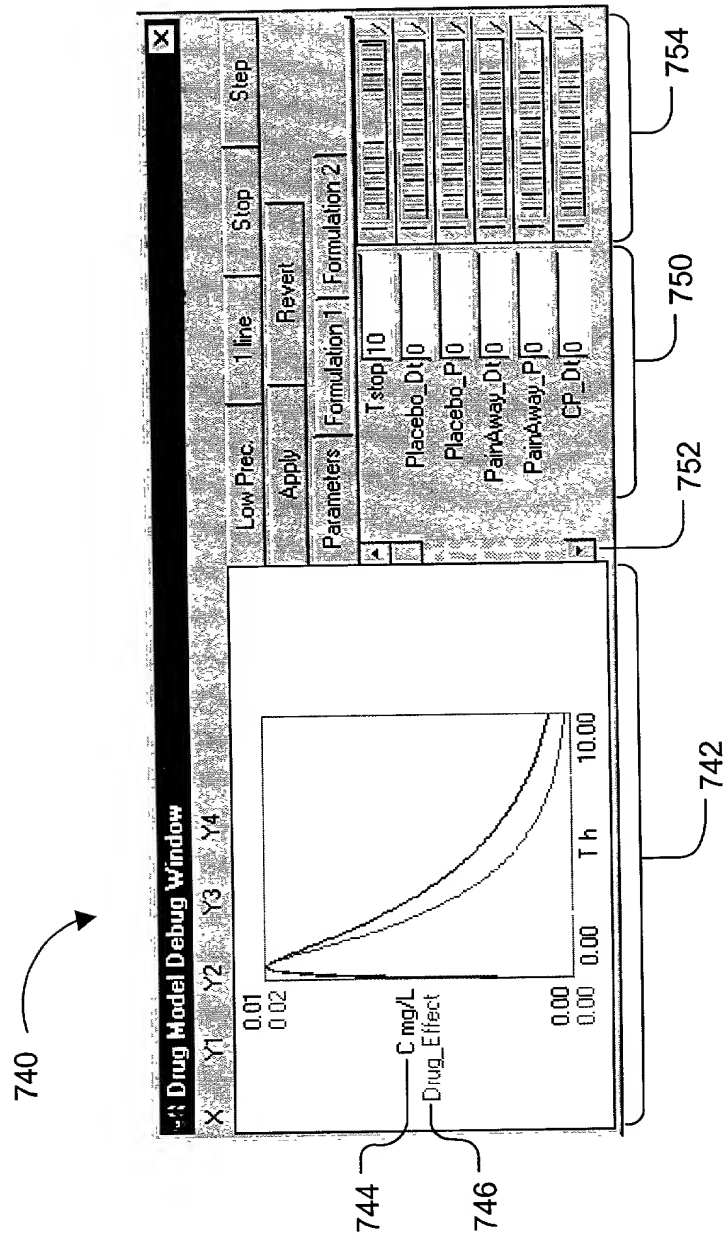
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FIG. 7B

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**FIG. 7C**

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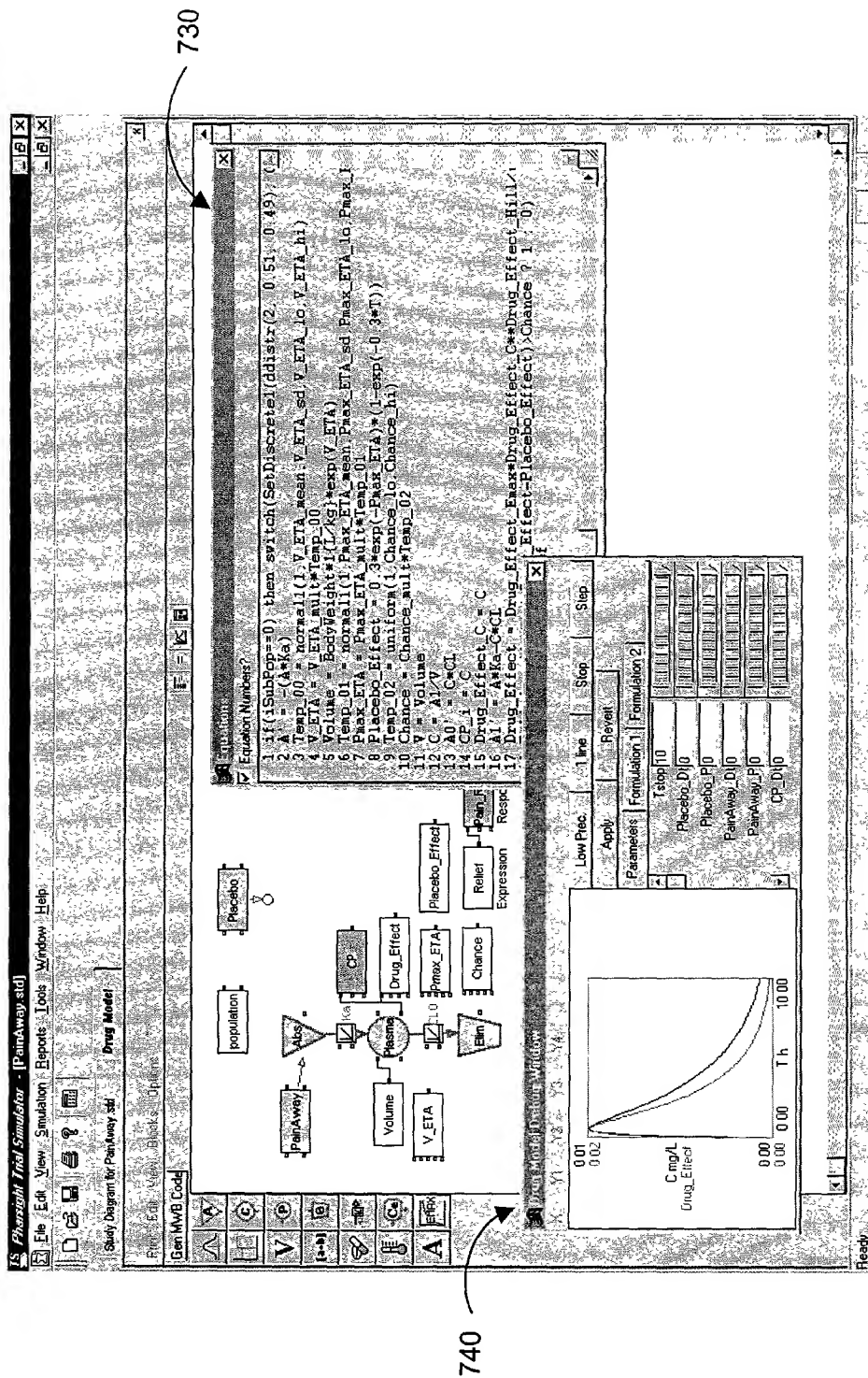


FIG. 7D

